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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/352,466	07/13/1999	VIRGINIA C BROUDY	A-195CDD	2305

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/352,466	BROUDY ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution on the merits of this application is again reopened on claims 71-92 in view of the Petition Decision mailed 30 April 2008.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 October 2007 has been entered.

3. Claims 1-70 are cancelled.

Claims 71-92 have been added.

4. Claims 71-92 are pending and under examination.

5. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

6. This Office Action contains New Grounds of rejections.

Objections/Rejections Withdrawn

7. The objection to The Brief Description of the Drawings because Figure 6 contains parts A and B, however, the Description of the Drawings for Figure 6 refers to "Figure 7A" and "Figure 7B" is withdrawn in view of the amendment to the specification filed 10/31/2007.

8. The rejection of claims 45-70 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating leukemia cells comprising administering to an anti-neoplastic therapeutic agent conjugated to the monoclonal antibody produced from the hybridoma cell line ATCC No. HB 10716 (i.e., monoclonal antibody SR-1) or antigen-binding fragments thereof, wherein the monoclonal antibody or antigen-binding fragments thereof bind the human c-kit receptor and inhibit binding of human stem cell factor to the human c-kit receptor therapeutic, thereby decreasing the growth rate of human c-kit bearing cancer cells, does not reasonably provide enablement for a method of treating just any cancer comprising administering to a

patient an anti-neoplastic therapeutic agent conjugated to just any monoclonal antibody or fragment thereof, wherein the monoclonal antibody or fragment thereof binds just any human stem cell factor receptor and inhibits binding of human stem cell factor to the human stem cell factor receptor, thereby decreasing the growth rate of human stem cell, factor receptor bearing cancer cells is withdrawn in view of the cancellation of the claims.

Applicant is advised that this rejection is not being applied to newly added claims 71-92 in view that the claims require the antibody or fragment thereof to bind OCIM1 cells and block binding of human stem cell factor to OCIM1 cells and the specification teaches the production of a monoclonal antibody (i.e., SR-1 produced by the hybridoma cell line ATCC No. HB 10716) by immunization with OCIM1 cells, wherein the antibody specifically binds the human c-kit receptor (see examples 2-4) and blocks binding of radiolabelled human stem cell factor to the human erythroleukemia cell line, OCIM1.

Objections/Rejections Maintained and New Grounds of Rejections

9. The objection to the specification at pg. 1, line 26 because the terms “murine”, “been” and “Cellular” are misspelled and require correction.

The response filed 10/31/2007 states that the spellings appear to be correct and have not been changed. This has been fully considered but is not found persuasive. The term murine is misspelled as “murin”, the term been is misspelled “be n” and the term Cellular is misspelled “C llular”. Applicants’ cooperation is again requested in correcting the typographical errors in the specification

Appropriate correction is required.

10. Claim 83 is objected to as not ending in a period.

Appropriate correction is required.

11. Claims 71-72, 81-82 and 87-92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 71-72 and 87-92 are indefinite in the recitation “leukemia therapeutic agent” in claims 71 and 87 and in the recitation of “solid tumor therapeutic agent” in claims 72 and 87. It is unclear what is contemplated by defining the therapeutic agents as a “leukemia therapeutic agent” or “solid tumor therapeutic agent", because the class of therapeutic agents are not defined as leukemia-specific or specific for solid tumor. The class of therapeutic agents recited in the claims is generic and non-specific in nature. While the linkage of the therapeutic agents to an antibody specific for an antigen on leukemia or solid tumor cell will target the therapeutic agent to a particular cell type, the particular therapeutic agents cannot be said to be specific for a particular cell type or cancer, i.e., "leukemia therapeutic agent". As written, one of skill in the art would not be reasonably apprised of the metes and bounds of the claims. Amending claims 71, 72 and 87 to recite "a therapeutic agent", would overcome this rejection, provided no new matter is introduced.

b. Claim 81 is indefinite in the recitation "monoclonal antibody or fragment thereof comprises a murine hypervariable region and a human constant and framework region” Those of skill in the art recognize a chimeric antibody to be an antibody in which both the heavy chain variable region (which comprises the three heavy chain CDRs) and the light chain variable region (which comprises the three light chain CDRs) of a rodent antibody or the human CDRs with other human framework regions are recombined with constant region sequences from a human antibody of a desired isotype (e.g., see Bendig M. M., Methods: A Companion to Methods in Enzymology, 8:83-93, 1995; see Figs. 1-3). Thus, one of skill in the art would not understand what is contemplated by a monoclonal antibody or fragment thereof that binds to OCIM1 cells and only comprises one variable region (“a murine variable region”) and only one human constant region (i.e., a CH1 region) and only one human framework region (i.e., FR1 region). Amending the claim to recite “comprises murine variable regions and human constant and

framework regions", would overcome this rejection, provided no new matter is introduced.

c. Claim 82 is indefinite in the recitation "monoclonal antibody or fragment thereof comprises a murine hypervariable region and a human constant and framework region". Those of skill in the art recognize a humanized antibody involves the substitution of all six CDRs (hypervariable regions) from a rodent antibody that binds an antigen of interest onto human frameworks and comprising constant regions for complete antibodies (e.g., see Bendig M. M., Methods: A Companion to Methods in Enzymology, 8:83-93, 1995; see Figs. 1-3). Thus, one of skill in the art would not understand what is contemplated by a monoclonal antibody or fragment thereof that binds to OCIM1 cells and only comprises one murine hypervariable region ("a murine hypervariable region") and only one human constant region (i.e., a CH1 region) and only one human framework region (i.e., FR1 region). Amending the claim to recite "comprises murine hypervariable regions and human constant and framework regions", would overcome this rejection, provided no new matter is introduced.

d. Claim 84 is indefinite in the recitation "monoclonal antibody or fragment thereof comprises a human monoclonal antibody". A human monoclonal antibody is merely one form of monoclonal antibody, and a monoclonal antibody would not comprise another monoclonal antibody, human or not. It is unclear what is contemplated by a monoclonal antibody comprises a human monoclonal antibody. Is the human monoclonal antibody the monoclonal antibody or not? Further, a fragment of a monoclonal antibody would not comprise a human monoclonal antibody, since a fragment of a monoclonal antibody would only comprise part of a monoclonal antibody. As written, one of skill in the art would not readily recognize what is meant by a monoclonal antibody or fragment thereof that comprises a human monoclonal antibody

12. Claims 71-92 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line having the exact chemical identity of the human erythroleukemia cell line, OCIM1, is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

The specification lacks complete deposit information for the deposit of the OCIM1 cell line. It is unclear whether cell lines possessing the identical properties of the OCIM1 cell line are known and publicly available or can be reproducibly isolated from nature without undue experimentation. It is noted that the instant specification discloses that the OCIM1 cell line has been described previously (specification at pg. 9). With respect to the OCIM1 cell line, there is no indication in the specification that the OCIM1 cell line is readily available to the public and the specification does not provide sufficient guidance or direction to assist one skilled in the art to make and/or use this cell line to produce and screen the claimed monoclonal antibodies of the claimed method.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed OCIM1 cell line, a suitable deposit is required for patent purposes, evidence of public availability of the claimed OCIM1 cell line or evidence of the reproducibility of the OCIM1 cell line without undue experimentation of the claimed vectors, is required.

Applicants are directed to the requirements and conditions of 37 CFR 1.801-1.809 for biological deposits.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record

who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of the OCIM cell line has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of the OCIM1 cell line is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

> (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:
> (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:
> (c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
> (d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

<u>If a deposit is made after the effective filing date of the application for patent</u> in the United States, a verified statement is required from a person in a position to

corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

13. Claims 74 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed 10/31/2008 has introduced NEW MATTER into the claims. Newly added claim 74 recites wherein the monoclonal antibody of the methods of claims 71 and 72 competes with the monoclonal antibody produced from hybridoma cell line ATCC No. HB 10716 for binding to OCIM1 cells. The response did not point out where support for newly added claim 74 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). After a review of the as filed disclosure, support for the subgenus of monoclonal antibodies that compete with the monoclonal antibody produced from hybridoma cell line ATCC No. HB 10716 for binding to OCIM1 cells cannot be found. Thus, instant claim 74 now recites limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in newly added claim 74, which did not appear in the specification, as

filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claim 74 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643